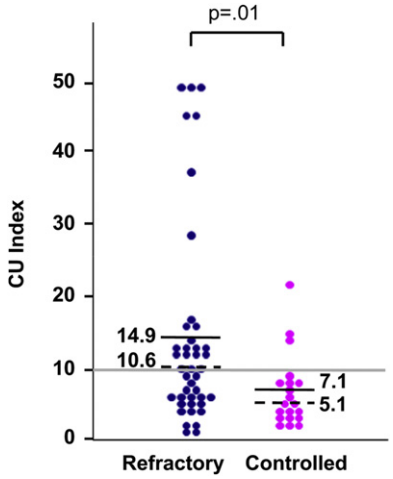

FIG 1. CU Index values for patients with CIU who were labeled as refractory or controlled with the use of antihistamines with or without LTRAs. Mean values are listed and represented by the *solid lines*. Median values are listed and represented by the *dashed line*. The *gray line* indicates the defined threshold of 10 for a positive CU Index value.

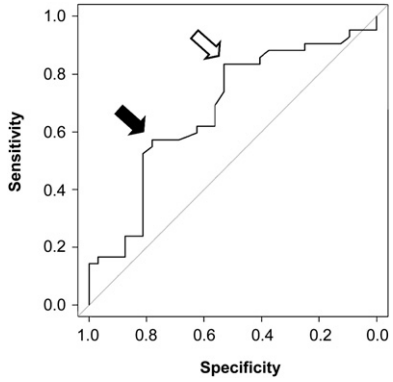

FIG 2. Receiver operating curve indicating the sensitivities and specificities for the optimized decision threshold value of 5.25 *(open arrow)* and the autoimmunity decision threshold of 10 *(solid arrow)*.

of between 5.25 and less than 10, 68% were refractory; and for patients with CU Index values of greater than or equal to 10, 88% were refractory (Fig 3). This suggests that almost 9 of 10 patients with a CU Index greater than or equal to 10 required more than antihistamine and LTRA therapy. Thus the CU Index could help guide whether a more aggressive level of medication will be required to achieve symptom control.

One limitation of this study is that it was retrospective and the patients were not assessed and managed according to a common protocol; patients were at most treated with twice the manufacturer's dose of nonsedating H_1-antihistamines and not 4 times the dose, as has been recently identified as effective.[9] Another limitation is that the determination of response to medications was based on a subjective evaluation of the medical record (by M. J. B. and R. K. V.) rather than a validated instrument, such as the Urticaria Activity Score.[10] Despite these limitations, our results suggest that the CU Index has implications for predicting disease severity and responsiveness to medications. A prospective study of patients with CIU is warranted to validate these findings and to further evaluate the clinical utility of the CU Index.

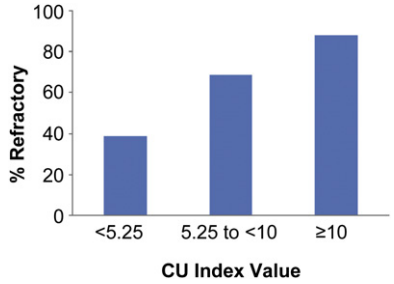

FIG 3. Percentage prevalence of patients refractory to antihistamines with or without LTRAs based on CU Index value ranges.

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Diagnosing IgE-mediated hypersensitivity to sesame by an immediate-reading "contact test" with sesame oil

To the Editor:

Sesame allergy has been reported as increasingly frequent in both adults and children,[1] in particular in Europe (2% to 4% of total food allergies).[2] This phenomenon may be a result of the

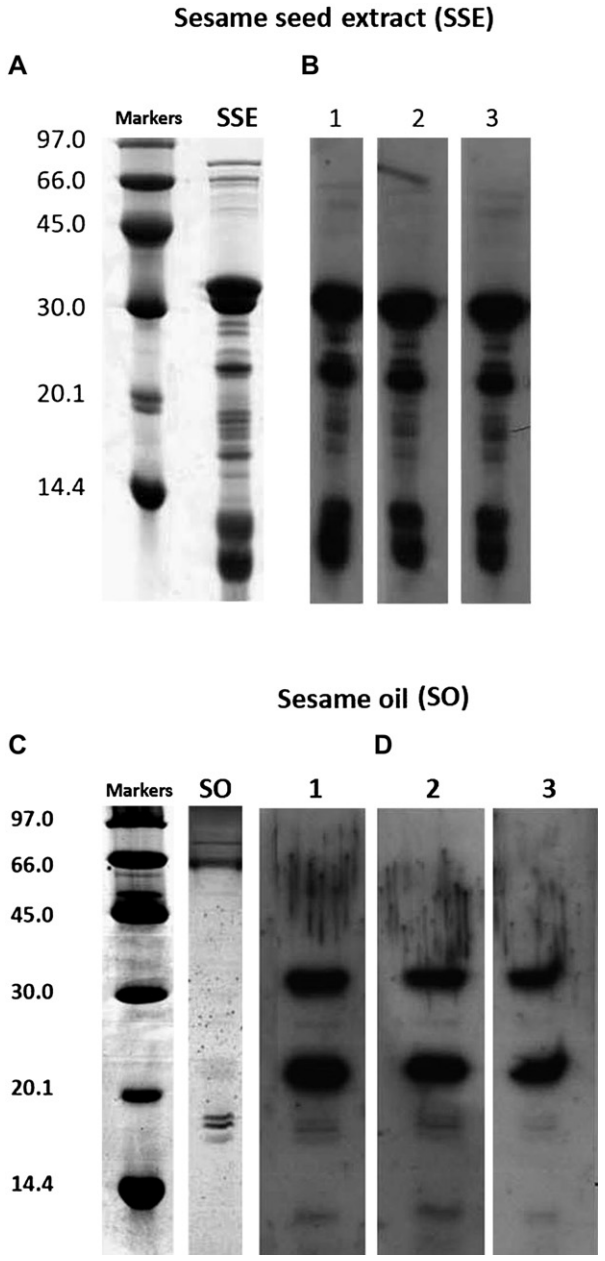

FIG 1. A, The SDS-PAGE in Coomassie stain with the sesame seed extract under reducing conditions (with β-mercaptoethanol). **B,** IgE reactivity of the patients' sera in Western blot with the sesame seed extract. **C,** The SDS-PAGE in silver stain with the sesame oil under reducing conditions (with β-mercaptoethanol). **D,** IgE reactivity of the patients' sera in Western blot with the sesame oil. *1,* Patient 1; *2,* patient 2; *3,* patient 3.

increased use of sesame in vegetarian dietary regimens and of the introduction of exotic foods.

Most literature data concerning sesame allergy are reports of single cases or case series. In a series of 9 patients with hypersensitivity reactions to sesame seeds, Kanny et al[3] described 2 patients who also had anaphylactic reactions to sesame oil. In these patients, an IgE-mediated hypersensitivity was diagnosed on the basis of positive responses to both skin prick tests (SPTs) with sesame seed flour and double-blind placebo-controlled food challenges. Two other cases of immediate hypersensitivity to sesame seeds and sesame-containing cosmetic oils have been described by Pecquet et al[4]: these subjects displayed negative results to SPTs with a commercial sesame extract but positive ones with crushed sesame seeds. In both studies,[3,4] specific IgE assays were negative. However, 2 studies[5,6] demonstrated that a titer of sesame-specific IgE lower than 0.35 kU_A/L is useful to rule out an IgE-mediated hypersensitivity to sesame. Nevertheless, according to Zavalkoff et al,[5] oral provocation tests should be offered to all patients to confirm the diagnosis of sesame allergy irrespective of SPT or sesame-specific IgE results, even though in patients with a sesame-specific IgE level <0.35 kU_A/L, the risk of an allergic reaction is extremely low. In this connection, cases of anaphylaxis have been reported in patients presenting negative results in both SPTs and specific IgE assays.[7]

In a study by Leduc et al,[1] which included SDS-PAGE immunoblotting of a purified oil body fraction, Ses i 4 and Ses i 5 (2 oleosins from sesame seeds) were recognized by the IgE from 29 of the 32 patients with hypersensitivity reactions to sesame. Six of them reported reactions to sesame oil and presented negative responses to both SPTs and specific IgE assays with sesame seeds. Thus, these authors[1] highlighted the need to improve the quality of sesame extract for diagnosis.

We report 3 cases of immediate reactions to sesame. Patient 1 was a 42-year-old man with 2 anaphylactic reactions after ingestion of breadsticks and candy, respectively; both products contained sesame. Patient 2 was a 28-year-old man with 2 urticarial and angioedematous reactions within 10 minutes after the ingestion of bread containing sesame seeds. Patient 3 was a 38-year-old man with an 8-year history of several urticarial and angioedematous reactions within 30 minutes after ingesting sesame-containing foods, such as bread, crackers, and products cooked in sesame oil. Case histories were not suggestive of any other food allergies or atopic manifestations. They underwent SPTs with a panel of 2 commercial extracts of food allergens including sesame (Stallergènes, Paris, France; ALK-Abelló, Madrid, Spain), with negative results.

Like Leduc et al,[1] we also performed SPTs with natural sesame seed crushed in saline. Patient 1 displayed an immediate response (maximum wheal diameter of 5 mm, surrounded by erythema), whereas patients 2 and 3 had a negative response. No sesame-specific IgE were detected in any patient (<0.10 kU_A/L, ImmunoCAP; Phadia, Uppsala, Sweden). SPTs with commercial sesame oil (Crudigno, Organic Oils Spa; Mugnano, Perugia, Italy) were performed on the volar side of the forearm; the drops of oil were wiped away with a paper tissue after the SPTs, which were negative. An immediate-reading "contact test" with sesame oil was performed by applying on the volar side of the forearm a square of filter paper (10 × 10 mm) dipped in sesame oil (Crudigno) and removing it after 20 minutes. On the contact side, patient 2 presented a wheal reaction the same size as the filter paper, whereas patients 1 and 3 presented several 4-mm-diameter wheals also involving the surrounding area (diameters 2 and 5 cm, respectively). Immediate-reading contact tests with 2 tolerated oils were also performed on each patient by applying on the volar side of the forearm a square of filter paper (10 × 10 mm) dipped in extra-virgin olive oil (Crudigno) and refined peanut oil (Dante Oil, Mataluni Spa; Montesarchio, Benevento, Italy), with negative results. The immediate-reading contact test with sesame oil was negative in 10 healthy subjects, 5 of whom used sesame-containing foods regularly in their diet.

As regards patients 2 and 3, considering negative results of *in vivo* and *in vitro* tests as well as the fact that they had not experienced severe reactions, an open food challenge was performed to firmly establish the diagnosis. In accordance with Kanny et al,[3] we administered increasing doses of sesame seeds (0.05, 0.5, 1, 5, and 10 g) every 30 minutes. Both patients experienced urticarial reactions: the first one 20 minutes after the dose of 0.5 g, the second 15 minutes after the dose of 1 g. Consequently, no oral provocation test with sesame oil was performed. We did not perform an oral provocation test in patient 1, because of the previous anaphylactic shock and positivity to SPTs with sesame seeds.

Specific IgE was further analyzed by immunoblot experiments with an extract of sesame seeds and sesame oil (Fig 1). All patients' sera (diluted 1:4 in PBS-Tween 0.5%) showed an IgE binding to several proteins of the oil bodies (membrane lipoproteins), such as oleosins (the band with molecular mass around 15-17 kDa).

To our knowledge, these are the first cases of hypersensitivity to sesame diagnosed by a simple immediate-reading contact test with sesame oil. Because oleosins are hydrophobic and can not be solubilized in normal saline, a negative prick-to-prick test with crushed sesame seeds is not sufficient to exclude sesame allergy, especially in subjects in whom specific IgE is directed prevalently to liposoluble proteins. For this reason, patients with histories of adverse reactions to sesame should also be tested with an immediate-reading "contact test" with sesame oil, in which oleosins are anchored onto the surface by its central hydrophobic domain and can easily penetrate the skin. Negative results in SPTs with sesame oil can be explained by the fact that the oil drops were wiped away immediately after testing and there was not enough time to allow oil to penetrate into the skin.

The data from Leduc et al[1] and our data indicate that sensitization to oleosins can play an etiologic role in some subjects with immediate reactions to sesame products. Therefore, sensitization to oleosins might constitute a diagnostic problem in both adults and children. In effect, even though all our patients were adults, one of the patients described by Leduc et al[1] was a 9-year-old girl.

Few data exist on the allergenicity of other vegetable oils. The presence of oleosins has been shown in some of them. In peanut oil, for example, the allergenicity of oleosins has been established,[8] even though commercially available, refined peanut oil has been proven to be well tolerated by most subjects with peanut allergy.[9] In effect, the major refined oils are not thought to induce symptoms in susceptible individuals.[10] There are commercial available crude and cold-pressed peanut oils that contain proteins. Sesame oil differs from the others because it is typically available as an unrefined, crude oil, which contains a significantly higher amount (3-13 μg/g) of proteins.[9,10]

Our immunoblot experiments detected serum-specific IgE to the oleosins contained in sesame oil. The sera of our patients also displayed a higher IgE-reactivity to other liposoluble proteins not yet characterized (Fig 1, *D*). Like oleosins, such lipoproteins are hydrophobic, and because they can not be solubilized in normal saline, they are not present in commercial extracts. Our data suggest that patients with histories of immediate reactions to sesame products and positive results in immediate-reading contact tests with sesame oil should be instructed to avoid all sesame products, including oil. However, further studies in larger samples are needed to confirm the usefulness of this immediate-reading contact test and to validate such advice.

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Ovalbumin content of 2010-2011 influenza vaccines

To the Editor:

Egg allergies affect an estimated 0.12% to 3.6% of the population.[1] Although exceedingly rare, some reports of anaphylaxis after immunization with the influenza vaccine in patients with egg allergy resulted in guidelines that make severe egg allergy a relative contraindication for immunization with these vaccines.[2]

The currently available practice parameter[3,4] for administration of influenza vaccines to patients with egg allergy recommends using a vaccine with known ovalbumin content of 1.2 μg/mL or less and administering it in 2 doses (10% of the dose followed in 30 minutes by the remaining 90%) or as a single dose without prior vaccine skin testing. This recommendation is partly based on a study by James et al[5] in 1998 that showed that 2-step dosing was safe, even in patients with a history of anaphylaxis to egg. No subjects experienced adverse reactions to vaccines containing as much as 1.2 μg/mL. Unfortunately, the specific egg protein content of any given year's influenza vaccines is not readily available.

Compared with reports[6] of influenza vaccines in the mid-1990s and early-2000s that contained up to 42 μg/mL ovalbumin,